STEREOCHEMICAL CRITERIA FOR POLYPEPTIDE AND PROTEIN CHAIN CONFORMATIONS

Part I. Evaluation of Helical Parameters

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1. INTRODUCTION

Proteins and polypeptides are long-chain polymers composed of a large number of peptide units \([-\text{CHR-CO-NH}]-\) linked together at the \(\alpha\)-carbon atoms. The configuration of such a chain will depend on the relative orientations of the two peptide units linked at each \(\alpha\)-carbon atom. If the configuration at each of the \(\alpha\)-carbon atoms is specified, then the conformation of the chain as a whole gets specified. In the next section, we shall discuss the notation that has been developed for denoting the configuration at an \(\alpha\)-carbon atom. However, it is clear that if this configuration is the same at every such carbon atom, then there will be a regular twisting of the structure from one residue to the next, and a helical structure would result. In this paper, we shall be mainly concerned with the nature and type of the helical conformations which arise as a result of such regular sequences of configurations, supposing that all such configurations are possible. In Part II, we shall consider the restrictions which arise from considerations of stereochemistry.

A regular helical structure composed of peptide units, as is the case with a polypeptide chain, may be specified by two parameters: (a) the number of units per turn \((n)\) which may be non-integral, and (b) the unit translation \((h)\), or the resolved height of a unit along the axis of the helix. We may take the unit translation to be always positive and denote the right- or left-handedness of the helix by a positive or negative sign respectively of \(n\). Instead of the number \(n\), one may use the unit twist \((\Delta)\) or the angle by which two neighbouring units are twisted with respect to each other about the axis of the helix. Taking the helix to be progressing vertically upwards, \(\Delta\) is positive, or counterclockwise, looking down upon the helix from above, for a right-handed helix, and \textit{vice versa} for a left-handed
helix. We have the obvious simple relation $n = 360/\Delta$, if $\Delta$ is measured in degrees.

The problem of polypeptide chain conformation has been examined by a number of earlier workers (Huggins, 1943; Bragg et al., 1950; Pauling et al., 1951; Donohue, 1953). The former two were interested only in integral helices. Although the latter two considered non-integral helices, they were mainly interested in conformations which were stabilized by a large number of hydrogen bonds. A general approach of the type discussed here does not appear to have been attempted earlier.

It should be mentioned that the present study is based on the well-known Pauling-Corey parameters for the peptide residue. According to this, the NH and CO groups are in the trans-configuration and the peptide residue is completely planar. The bond lengths and the bond angles of the planar peptide residue are taken to be those given by Corey and Pauling (1953). These are shown in Fig. 1.

2. GENERAL PRINCIPLES

To represent the various possible conformations of the polypeptide chain, the following notation has been found to be convenient. The two planar peptide groups linked at an $\alpha$-carbon atom are in principle capable of free rotation about the two single bonds $\text{N}--\alpha\text{C}$ and $\alpha\text{C}--\text{C}'$ meeting at the $\alpha$-carbon atom. Designating the atoms of the first peptide group by $H_1$ $C_1$ $C_1'--N_1--C_2$ and those of the second group by $C_2--C_2'--N_2--C_3$, the two possible free rotations are about the bond $N_1--C_2$ of the first group and about the bond $C_2--C_2'$ of the second group. These two rotations are represented by $\phi$ and $\phi'$ respectively and a particular configuration at the $\alpha$-carbon atom $C_2$ will be denoted by the pair of dihedral angles ($\phi$, $\phi'$). The initial configuration, i.e., the one with $\phi = \phi' = 0$ is taken to be that in which the planes of the two peptide groups lie in the plane $N_1C_2C_2'$ (which is independent of the rotations of the two groups), with the two NH groups close to each other, as shown in Fig. 2. The angles of rotation $\phi$ and $\phi'$ are taken to be positive for an anticlockwise rotation of the two groups viewed along $N_1--C_2$ and $C_2--C_2'$ respectively. The angles $\phi$ and $\phi'$ can take up any value between $0^\circ$ and $360^\circ$ and a combination ($\phi$, $\phi'$) uniquely specifies a regular helical structure. This paper is mainly concerned with the evaluation of the helical parameters $n$ and $h$ for a given combination ($\phi$, $\phi'$).